REMARKS/ARGUMENTS

Reconsideration and withdrawal of the rejections of the present application are respectfully requested in view of the amendments to the claims and remarks presented herewith, which place the application into condition for allowance.

Status of the Claims and Formal Matters

Claims 16-21, 23, and 35-44 were previously withdrawn. Claims 24 and 34 have been cancelled herewith. Claims 1, 12, 13, 14, 22, 25, 27, 28, 29, 32 and 33 have been amended herewith, without prejudice, and solely to expedite prosecution pursuant to the U.S. Patent and Trademark Office Business Goals (65 Fed. Reg. 54604 (September 8, 2000)). Applicants respectfully assert the right to reclaim withdrawn or cancelled subject matter in co-pending applications.

Specifically, claim 1 (the only independent claim after the amendments here) has been amended to recite that upon breaking the emulsion, the amplified template-carrying beads are released away from amplification reaction solution, those beads are enriched for by removing beads to which no nucleic acid is bound, and then the enriched amplified template-carrying beads are distributed onto an array. This is supported in the specification as filed, e.g., at page 5, lines 7-19 and page 14, line 20 to page 19, line 17. Claims 12, 13, 14, 25, 32 and 33 have been amended for clarity or to correct typographical errors. Claim 22 has been amended to depend from claim 1 (adding the step of sequencing the nucleic acid templates on the array). No new matter has been introduced by these amendments. Support for the amendments can be found throughout the specification as originally filed.

Rejections under 35 U.S.C. §103(a)

Claims 1-3, 6-15, 22, 24, 25, 27, 28, 32, and 33 were rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Griffiths (U.S. Patent Application Publication No. 20020119459; herein "Griffiths") in view of Andreadis et al. (Nucl. Acids Res. (2000) 28: e5, pp. i-viii; herein "Andreadis") and further in view of Wangh et al. (U.S. Patent Publication No.

20040053254; herein "Wangh") and Fan et al. (Anal. Chem (1999) 71: 4851-4859; "Fan"). [1/] According to the Office Action, it would allegedly have been *prima facie* obvious to one having ordinary skill in the art to combine the method of Griffiths for amplifying nucleic acids in a microcapsule such as a water-in-oil emulsion on the surface of a bead contained within the emulsion with the methods of Fan for binding at least 1 million copies of a primer or target to the bead and extending at least 100,000 bead-bound complementary strands, and extending the primers with the methods of Andreadis and Wangh for performing asymmetric PCR using two populations of a first primer, one attached to a solid surface and one in lower concentration in solution, since the primer in solution can be used to exhaustion to perform the initial rounds of amplification on the target nucleic acid in combination with the second primer, while the resulting extension products can be further amplified in the solid-phase to generate products immobilized on the bead. Applicants disagree.

None of the cited art, taken alone or in combination, describes asymmetric nucleic acid amplification using microreactors formed from a water-in-oil emulsion, driving the amplified template to beads, breaking the emulsion to recover the beads and then enriching for those beads that have amplified template attached thereto (away from "zero" beads to which no nucleic acid is bound) and distributing the enriched population of amplified template-carrying beads to an array. The claimed method is highly commercially desirable as it permits the removal of "zero" beads that do not contain any amplified template nucleic acid. This means that the skilled artisan can now produce a highly enriched population of beads that have amplicon bound thereon. Such enriched populations of amplicon may be used for distribution on an array for a variety of analyses, including, e.g., sequencing. The ability to enrich for amplicon containing beads and

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[1/] Claim 29 was rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Griffiths in view of Andreadis, Wangh, Fan, and further in view of Jurinke et al. (U.S. Patent No. 6,303,309; herein "Jurinke"). The Office Action contends that it would allegedly have been *prima facie* obvious to one having ordinary skill in the art to combine the methods of Griffiths, Andreadis, Wangh and Fan for amplifying nucleic acids on a bead within a microcapsule, such as a water-in-oil emulsion, using a non-symmetric PCR with that of Jurinke for purification of PCR products using solid supports, such as magnetic or Sepharose beads, since the use of such beads, because of the stability of the biotin-streptavidin complex, allows further purification and extensive washing to remove all excessive reaction components prior to final recovery of the final PCR product. Applicants respectfully traverse for the same reasons discussed above.

eliminate the zero beads has tremendous commercial benefits, as no (or few) locations on the array are "wasted" by being occupied by a zero bead that does not produce any signal in a sequencing reaction or other assay for characteristics of the amplified nucleic acids.

Claim 34 was rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Griffiths in view of Andreadis, Fan, and further in view of Nakano et al. (J. Biotech. (2003) 102: 117-124; "Nakano"). Claim 34 has been cancelled herewith – the rejection is moot.

CONCLUSION

This case is believed to be in condition for allowance. If any discussion regarding this Response is desired, the Examiner is respectfully urged to contact the undersigned at the number given below, and is assured of full cooperation in progressing the application to allowance.

If any additional fees are required or if any funds are due, the USPTO is authorized to charge or credit Deposit Account Number **50-0311**, Customer Number: **35437**, Reference Number: **21465-508001US**.

Respectfully submitted,

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